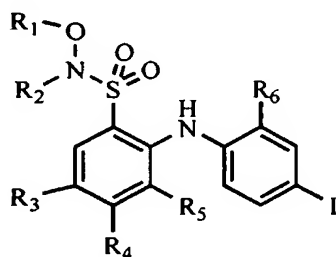


CLAIMS

1. A method for treating chronic pain, said method comprising administering to a subject in need of such treatment a composition comprising a MEK inhibitor selected from: a compound of formula (I):



(I)

R_1 is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (phenyl)C₁₋₄ alkyl, (phenyl)C₃₋₄ alkenyl, (phenyl)C₃₋₄ alkynyl, (C₃₋₈ cycloalkyl)-C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkenyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkynyl, (CH₂)₂₋₄ OR_C or (CH₂)₂₋₄ NR_CR_D ;

R_2 is H, C₁₋₄ alkyl, phenyl, C₃₋₆ cycloalkyl, C₃₋₆ heterocyclic radical, or (C₃₋₆ cycloalkyl) methyl;

each of R_3 and R_4 is independently selected from H, F, NO₂, Br and Cl;

R_5 is selected from H and F;

R_6 is H, F, Cl or CH₃;

each of R_C and R_D is independently selected from H, C₁₋₄ alkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, and phenyl; or NR_CR_D may be a piperidino, morpholino, or N-(C₁₋₆ alkyl)piperazino ring;

wherein each hydrocarbon radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, hydroxyl, amino, (amino)sulfonyl, and NO₂; and

- 5 wherein each heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₄ alkyl, C₃₋₆ cycloalkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO₂, wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 2
10 substituents independently selected from halo, C₁₋₂ alkyl, hydroxyl, amino, and NO₂;

or a pharmaceutically acceptable salt or C₁₋₈ ester thereof.

15

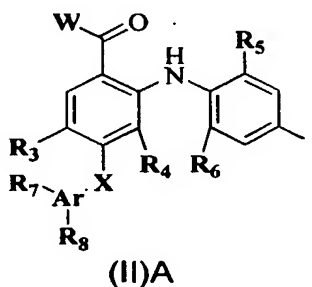
2. The method of claim 1, wherein said chronic pain is selected from neuropathic pain, idiopathic pain, and pain associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.
3. The method of claim 2, wherein said chronic pain is a type of
20 neuropathic pain.
4. The method of claim 3, wherein said neuropathic pain is associated with one of the following: inflammation, postoperative pain, phantom limb pain, burn pain, gout, trigeminal neuralgia, acute herpetic and postherpetic pain, causalgia, diabetic neuropathy, plexus avulsion, neuroma, vasculitis,
25 viral infection, crush injury, constriction injury, tissue injury, limb amputation, post-operative pain, arthritis pain, and any other nerve injury between the peripheral nervous system and the central nervous system, inclusively.
5. The method of claim 2, wherein said chronic pain is associated with
30 chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

6. The method of claim 2, wherein said chronic pain is associated with idiopathic pain.
- 5 7. The method of claim 1, wherein said chronic pain is associated with inflammation.
8. The method of claim 1, wherein said chronic pain is associated with arthritis.
- 10 9. The method of claim 1, wherein said chronic pain is associated with post-operative pain.
- 15 10. The method of claim 1, wherein R_3 is bromo or chloro.
11. The method of claim 1, wherein R_4 is fluoro.
12. The method of claim 1, wherein R_5 is H.
- 20 13. The method of claim 12, wherein each of R_4 and R_5 is H.
14. The method of claim 1, wherein each of R_4 and R_5 is fluoro.
- 25 15. The method of claim 14, wherein R_3 is bromo.
16. The method of claim 14, wherein R_3 is fluoro.
17. The method of claim 1, wherein R_4 is nitro.
- 30 18. The method of claim 16, wherein R_5 is H.

19. The method of claim 1, wherein R_6 is chloro.
20. The method of claim 1, wherein R_6 is methyl.
- 5 21. The method of claim 1, wherein R_1 is H or C_{1-4} alkyl, and R_2 is H.
22. The method of claim 1, wherein R_1 is (C_{3-6} cycloalkyl)methyl.
23. The method of claim 1, wherein R_1 is H.
- 10 24. The method of claim 1, wherein R_1 is $(CH_2)_{2-4}OR_C$ or $(CH_2)_{2-4}NR_CR_D$.
25. The method of claim 1, wherein said MEK inhibitor has a structure selected from: 4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonic acid; 4-fluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; N-cyclopropylmethoxy-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; 3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonic acid; 3,4-difluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; 3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonic acid; 3,4,5-trifluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; N-cyclopropylmethoxy-3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; 5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonic acid; 5-bromo-3,4-difluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; 5-bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; 2-(4-iodo-2-methyl-phenylamino)-4-nitro-benzenesulfonic acid; N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-4-nitro-benzenesulfonamide; and
- 25 30 N-cyclopropylmethoxy-2-(4-iodo-2-methyl-phenylamino)-4-nitro-benzenesulfonamide.

26. The method of claim 1, wherein said MEK inhibitor has a structure selected from: 2-(2-chloro-4-iodo-phenylamino)-4-fluoro-benzenesulfonic acid; 2-(2-chloro-4-iodo-phenylamino)-4-fluoro-N-hydroxy-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-fluoro-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-benzenesulfonic acid; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-3,4,5-trifluoro-benzenesulfonic acid; 2-(2-chloro-4-iodo-phenylamino)-3,4,5-trifluoro-N-hydroxy-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4,5-trifluoro-benzenesulfonamide; 5-bromo-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-benzenesulfonic acid; 5-bromo-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzenesulfonamide; 5-bromo-2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-4-nitro-benzenesulfonic acid; 2-(2-chloro-4-iodo-phenylamino)-N-hydroxy-4-nitro-benzenesulfonamide; and 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-nitro-benzenesulfonamide.

27. A method for treating chronic pain, said method comprising administering to a subject in need of such treatment a composition comprising a MEK inhibitor selected from a compound having the formula (II)A:



W is OR_1 , NR_2OR_1 , NR_AR_B , $NR_2NR_AR_B$, or $NR_2(CH_2)_{2-4}NR_AR_B$;

R_1 is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (phenyl)C₁₋₄ alkyl, (phenyl)C₃₋₄ alkenyl, (phenyl)C₃₋₄ alkynyl, (C₃₋₈ cycloalkyl)-C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkenyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkynyl or $(CH_2)_{2-4}NR_AR_B$;

R_2 is H, phenyl, C₁₋₄ alkyl, C₃₋₄ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, or (C₃₋₈ cycloalkyl)-C₁₋₄ alkyl;

R_A is H, C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C₁₋₄ alkyl, (aminosulfonyl)C₁₋₆ alkyl, (aminosulfonyl)C₃₋₆ cycloalkyl, or [(aminosulfonyl)C₃₋₆ cycloalkyl]C₁₋₄ alkyl;

R_B is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, or C₆₋₈ aryl;

R_3 is halo, NO_2 , $SO_2NR_I(CH_2)_{2-4}NR_ER_F$, $SO_2NR_IR_K$ or $(CO)T$;

T is C₁₋₈ alkyl, C₃₋₈ cycloalkyl, $(NR_ER_F)C_{1-4}$ alkyl, OR_F , $NR_I(CH_2)_{2-4}NR_ER_F$, or NR_ER_F ;

R_4 is H or F;

R_5 is H, methyl, halo, or NO_2 ;

R_6 is H, methyl, halo, or NO_2 ;

Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

- each of R_7 and R_8 is independently selected from H, halo, C_{1-4} alkyl, $SO_2NR_J(CH_2)_{2-4}NR_GR_H$, $(CO)(CH_2)_{2-4}NR_GR_H$, $(CO)NR_J(CH_2)_{2-4}NR_GR_H$,
5 $(CO)O(CH_2)_{2-4}NR_GR_H$, $SO_2NR_GR_H$, and $(CO)NR_GR_H$; provided that where Ar is a pyridyl, each of R_7 and R_8 is H;

- each of R_C , R_D , R_E , R_F , R_G , and R_H is independently selected from H, C_{1-4} alkyl,
10 C_{3-4} alkenyl, C_{3-4} alkynyl, C_{3-6} cycloalkyl, and phenyl; each of NR_CR_D , NR_ER_F , and NR_GR_H can also be independently morpholinyl, piperazinyl, pyrrolidinyl, or piperadynyl;

- each of R_I and R_J is independently H, methyl, or ethyl;

15

R_K is C_{1-4} alkyl, C_{3-4} alkenyl, C_{3-4} alkynyl, C_{3-6} cycloalkyl, or phenyl;

X is O, S, or NH; and

- 20 wherein each hydrocarbon radical or heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO_2 , wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 2
25 substituents independently selected from halo, C_{1-2} alkyl, hydroxyl, amino, and NO_2 ;

or a pharmaceutically acceptable salt or C_{1-7} ester thereof.

28. The method of claim 27, wherein said chronic pain is selected from neuropathic pain, idiopathic pain, and pain associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

5 29. The method of claim 28, wherein said chronic pain is a type of neuropathic pain.

30. The method of claim 29, wherein said neuropathic pain is associated with one of the following: inflammation, postoperative pain, phantom limb pain, burn pain, gout, trigeminal neuralgia, acute herpetic and postherpetic pain, causalgia, diabetic neuropathy, plexus avulsion, neuroma, 10 vasculitis, viral infection, crush injury, constriction injury, tissue injury, limb amputation, post-operative pain, arthritis pain, and any other nerve injury between the peripheral nervous system and the central nervous system, inclusively.

15 31. The method of claim 28, wherein said chronic pain is associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

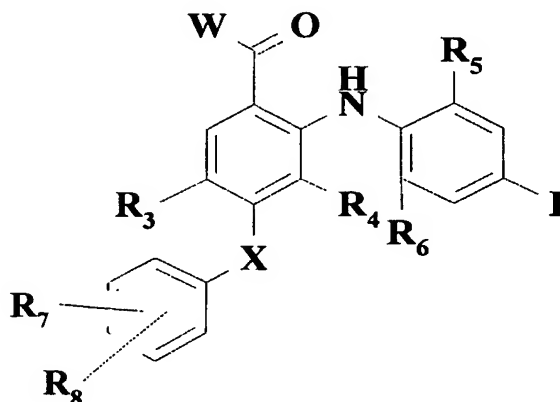
20 32. The method of claim 28, wherein said chronic pain is associated with idiopathic pain.

33. The method of claim 27, wherein said chronic pain is associated with inflammation.

25 34. The method of claim 27, wherein said chronic pain is associated with arthritis.

35. The method of claim 27, wherein said chronic pain is associated with post-operative pain.

36. A method of claim 27, having the following formula (I)A:



(I)A

5 wherein

W is OR_1 , NR_2OR_1 , NR_AR_B , $NR_2NR_AR_B$, or $NR_2(CH_2)_{2-4}NR_AR_B$;

10 R_1 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, C_{3-8} cycloalkyl, phenyl, (phenyl) C_{1-4} alkyl, (phenyl) C_{3-4} alkenyl, (phenyl) C_{3-4} alkynyl, (C_{3-8} cycloalkyl)- C_{1-4} alkyl, (C_{3-8} cycloalkyl) C_{3-4} alkenyl, (C_{3-8} cycloalkyl) C_{3-4} alkynyl, C_{3-8} heterocyclic radical, (C_{3-8} heterocyclic radical) C_{1-4} alkyl, (C_{3-8} heterocyclic radical) C_{3-4} alkenyl, (C_{3-8} heterocyclic radical) C_{3-4} alkynyl or $(CH_2)_{2-4}NR_AR_B$;

15

R_2 is H, phenyl, C_{1-4} alkyl, C_{3-4} alkenyl, C_{3-8} alkynyl, C_{3-8} cycloalkyl, or (C_{3-8} cycloalkyl)- C_{1-4} alkyl;

20 R_A is H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, C_{3-8} cycloalkyl, phenyl, (C_{3-8} cycloalkyl) C_{1-4} alkyl, (C_{3-8} cycloalkyl) C_{3-4} alkenyl, (C_{3-8} cycloalkyl) C_{3-4} alkynyl, C_{3-8} heterocyclic radical, (C_{3-8} heterocyclic radical) C_{1-4} alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl] C_{1-4} alkyl, (aminosulfonyl) C_{1-6}

alkyl, (aminosulfonyl)C₃₋₆ cycloalkyl, or [(aminosulfonyl)C₃₋₆ cycloalkyl]C₁₋₄ alkyl;

R_B is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, or C₆₋₈ aryl;

R₃ is halo, NO₂, SO₂NR_I(CH₂)₂₋₄NR_ER_F, SO₂NR_IR_K or (CO)T;

T is C₁₋₈ alkyl, C₃₋₈ cycloalkyl, (NR_ER_F)C₁₋₄ alkyl, OR_F, NR_I(CH₂)₂₋₄NR_ER_F, or NR_ER_F;

R₄ is H or F;

R₅ is H, methyl, halo, or NO₂;

R₆ is H, methyl, halo, or NO₂;

each of R₇ and R₈ is independently selected from H, halo, C₁₋₄ alkyl, SO₂NR_J(CH₂)₂₋₄NR_GR_H, (CO)(CH₂)₂₋₄NR_GR_H, (CO)NR_J(CH₂)₂₋₄NR_GR_H, (CO)O(CH₂)₂₋₄NR_GR_H, SO₂NR_GR_H, and (CO)NR_GR_H;

each of R_C, R_D, R_E, R_F, R_G, and R_H is independently selected from H, C₁₋₄ alkyl,

C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, and phenyl; each of NR_CR_D, NR_ER_F, and NR_GR_H can also be independently morpholinyl, piperazinyl, pyrrolidinyl, or piperadiny;

each of R_I and R_J is independently H, methyl, or ethyl;

R_K is C₁₋₄ alkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, or phenyl;

X is O, S, or NH; and

wherein each hydrocarbon radical or heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₄ alkyl, C₃₋₆ cycloalkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO₂, wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 2 substituents independently selected from halo, C₁₋₂ alkyl, hydroxyl, amino, and NO₂;

or a pharmaceutically acceptable salt or C₁₋₇ ester thereof.

10

37. A method of claim 27, wherein R₃ is NO₂.

38. A method of claim 27, wherein R₄ is fluoro.

15

39. A method of claim 27, wherein each of R₃ and R₄ is independently selected from H and fluoro.

40. A method of claim 27, wherein R₅ is methyl, fluoro, or chloro.

20

41. A method of claim 27, wherein R₆ is methyl, chloro, fluoro, nitro, or hydrogen.

42. A method of claim 41, wherein R₆ is H.

25

43. A method of claim 41, wherein R₆ is fluoro.

44. A method of claim 27, wherein R_K is methyl or ethyl.

30

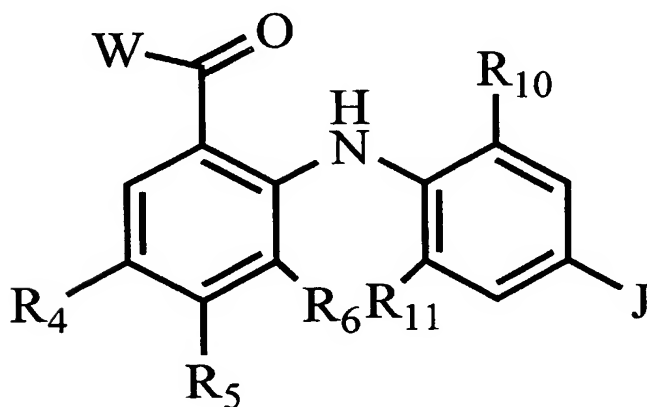
45. A method of claim 27, wherein R₁ is H, methyl, ethyl, propyl, isopropyl, isobutyl, benzyl, phenyl, phenethyl, allyl, C₂₋₅ alkenyl, C₃₋₆ cycloalkyl, (C₃₋₅ cycloalkyl)C₁₋₂ alkyl, (C₃₋₅ heterocyclic radical)C₁₋₂ alkyl, or (CH₂)₂₋₄ NR_CR_D.

46. A method of claim 45, wherein R_1 is H or (C₃₋₄ cycloalkyl)-C₁₋₂ alkyl.
- 5 47. A method of claim 27, wherein R_2 is H or methyl.
48. A method of claim 27, wherein R_A has at least one hydroxyl substituent.
- 10 49. A method of claim 27, wherein R_A is H, methyl, ethyl, isobutyl, hydroxyethyl, phenyl, 2-piperidin-1-yl-ethyl, 2,3-dihydroxy-propyl, 3-[4-(2-hydroxyethyl)-piperazin-1-yl]-propyl, 2-pyrrolidin-1-yl-ethyl, or 2-diethylamino-ethyl; and R_B is H; or where R_B is methyl and R_A is phenyl.
- 15 50. A method of claim 27, wherein W is NR_AR_B or $NR_2NR_AR_B$.
51. A method of claim 27, wherein W is $NR_2(CH_2)_{2-4}NR_AR_B$ or $O(CH_2)_{2-3}NR_AR_B$.
- 20 52. A method of claim 27, wherein W is NR_2OR_1 .
53. A method of claim 27, wherein W is OR_B .
54. A method of claim 27, wherein R_7 is in the para position relative
25 to X.
55. A method of claim 54, wherein R_7 is iodo.
56. A method of claim 27, wherein R_8 is in the ortho position relative
30 to X.

57. A method of claim 27 having the formula 2,4-bis-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-benzoic acid.

58. A method of claim 27, wherein said MEK inhibitor has a
 5 structure selected from: 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-(4-sulfamoyl-phenylamino)-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-phenylamino-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-phenoxy-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-phenylsulfanyl-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-
 10 3-fluoro-4-(methyl-phenyl-amino)-5-nitro-benzoic acid; benzamide, 2-[(2-chloro-4-iodophenyl)amino]-3-fluoro-N-hydroxy-4-[[4-[(2-hydroxyethyl)amino]-carbonyl]phenyl]amino]-5-nitro-; benzamide, 2-[(2-chloro-4-iodophenyl)amino]-4-[[4-[(dimethylamino)carbonyl]phenyl]amino]-3-fluoro-N-hydroxy-5-nitro-; 2-(2-chloro-4-iodo-phenylamino)-3,5-difluoro-4-phenylamino-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-(3-sulfamoyl-phenylamino)-
 15 benzoic acid; and 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-(2-sulfamoyl-phenylamino)-benzoic acid; and the corresponding hydroxamic acids and cyclopropylmethyl hydroxamates.

20 59. A method for treating chronic pain, said method comprising administering to a subject in need of such treatment a composition comprising a MEK inhibitor selected from a compound of formula (I)B:



(I)B

25

wherein

- 5 W is OR_1 , NR_2OR_1 , NR_AR_B , $NR_2NR_AR_B$, $O(CH_2)_{1-4}NR_AR_B$, or $NR_2(CH_2)_{1-4}NR_AR_B$;
 $O(CH_2)_{1-4}OR_1$, or $NR_2(CH_2)_{1-4}OR_1$;

- 10 R_1 is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (phenyl)C₁₋₄ alkyl, (phenyl)C₃₋₄ alkenyl, (phenyl)C₃₋₄ alkynyl, (C₃₋₈ cycloalkyl)-
 C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkenyl, or (C₃₋₈ heterocyclic radical)C₃₋₄ alkynyl;

- 15 each of R_2 and R_3 is independently H, phenyl, C₁₋₄ alkyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, or (C₃₋₈ cycloalkyl)C₁₋₄ alkyl;

- 20 each of R_4 , R_5 and R_6 is independently H, Cl, F, or Br;

- R_A is H, C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C₁₋₄ alkyl, (aminosulfonyl)C₁₋₆ alkyl, (aminosulfonyl)C₃₋₆ cycloalkyl, or [(aminosulfonyl)C₃₋₆ cycloalkyl]C₁₋₄ alkyl;

- R_B is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, or phenyl;
- 30 J is SR_C , OR_C , SO_2R_C , SOR_C , SO_2NR_DRE , C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, C₅₋₈ cycloalkenyl, phenyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl,

(C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, -M'E'G', (heterocyclic radical)-M'-E'-G', or (cycloalkyl)-M'-E'-G';

5 M' is O, SO, SO₂, NR_E, (CO)NR_E, NR_E(CO), SO₂NR_E, NR_ESO₂, or CH₂;

E' is absent (a covalent bond), (CH₂)₁₋₄ or (CH₂)_mO(CH₂)_p where 1 ≤ (each of m and p independently) ≤ 3 and 2 ≤ (m + p) ≤ 4;

10

G' is OR₃, SO₂R_C, or NR_FR_G; provided that where p = 1, then G' is H;

each of R_C, R_D, R_E, R_F and R_G is independently selected from H, C₁₋₆ alkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, C₃₋₆ heterocyclic radical,
15 and phenyl; NR_FR_G and NR_DR_E can each also independently be selected from morpholinyl, pyrazinyl, piperazinyl, pyrrolidinyl, or piperadinyl;

R₁₀ is H, C₁₋₄ alkyl, halo, NO₂, or SO₂NR_HR_i; and

20 R₁₁ is H, halo, or NO₂;

wherein each hydrocarbon radical or heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₄ alkyl, C₃₋₆ cycloalkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, phenyl, hydroxy,
25 amino, (amino)sulfonyl, and NO₂, wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₂ alkyl, hydroxy, amino, and NO₂;

30 or a pharmaceutically acceptable salt or C₁₋₇ ester thereof.

60. The method of claim 59, wherein said chronic pain is selected from neuropathic pain, idiopathic pain, and pain associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

5 61. The method of claim 60, wherein said chronic pain is a type of neuropathic pain.

62. The method of claim 61, wherein said neuropathic pain is associated with one of the following: inflammation, postoperative pain, phantom limb pain, burn pain, gout, trigeminal neuralgia, acute herpetic and postherpetic pain, causalgia, diabetic neuropathy, plexus avulsion, neuroma,
10 vasculitis, viral infection, crush injury, constriction injury, tissue injury, limb amputation, post-operative pain, arthritis pain, and any other nerve injury between the peripheral nervous system and the central nervous system, inclusively.

15 63. The method of claim 60, wherein said chronic pain is associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

20 64. The method of claim 60, wherein said chronic pain is associated with idiopathic pain.

65. The method of claim 59, wherein said chronic pain is associated with inflammation.

25 66. The method of claim 59, wherein said chronic pain is associated with arthritis.

67. The method of claim 59, wherein said chronic pain is associated with post-operative pain.

30 68. A method of claim 59, wherein R_C is C_{1-2} alkyl.

69. A method of claim 59, wherein W is OH.
70. A method of claim 59, wherein W is NHOH.
71. A method of claim 59, wherein W is NHO(cyclopropylmethyl).
72. A method of claim 59, wherein R₁₀ is methyl or chloro.
73. A method of claim 59, where R₁₁ is fluoro.
74. A method of claim 59, where R₁₁ is H.
75. A method of claim 59, wherein J is trihalomethyl or methylthio.
76. A method of claim 59, wherein J is 1,2,5-thiadiazol-3-yl.
77. A method of claim 59, wherein J is SO₂CH₃.
78. A method of claim 59, wherein J is SOCH₃.
79. A method of claim 59, wherein J is C₂₋₈ alkynyl where the triple bond is between the carbon atoms alpha and beta to the phenyl group.
80. A method of claim 59, wherein R₁ has at least one hydroxy substituent.
81. A method of claim 59, wherein R₁ is H, methyl, ethyl, propyl, isopropyl, isobutyl, benzyl, phenethyl, allyl, C₃₋₅ alkenyl, C₃₋₅ alkynyl, C₃₋₆ cycloalkyl, (C₃₋₅ cycloalkyl)C₁₋₂ alkyl, or (C₃₋₅ heterocyclic radical)-C₁₋₂ alkyl.

82. A method of claim 59, wherein R_1 is H or (C₃₋₄ cycloalkyl)-C₁₋₂ alkyl.

83. A method of claim 59, wherein R_2 is H, methyl, C₃₋₄ alkynyl, C₃₋₅ cycloalkyl, or (C₃₋₅ cycloalkyl)methyl.

84. A method of claim 59, wherein R_A is H, methyl, ethyl, isobutyl, hydroxyethyl, hydroxypropyl, cyclopropylmethyl, cyclobutylmethyl, C₂₋₄ alkynyl, phenyl, 2-piperidin-1-yl-ethyl, 2,3-dihydroxy-propyl, 3-[4-(2-hydroxyethyl)-piperazin-1-yl]-propyl, 2-pyrrolidin-1-yl-ethyl, or 2-diethylamino-ethyl; and R_B is H; or where R_B is methyl and R_A is phenyl.

85. A method of claim 59, wherein each of R_4 and R_6 is H, and R_5 is F.

86. A method of claim 59, wherein each of R_4 , R_5 , and R_6 is F.

87. A method of claim 59, wherein each of R_4 and R_5 is F and R_6 is Br.

88. A method of claim 59, wherein R_5 is F.

89. A method of claim 59, wherein said MEK inhibitor has a structure selected from: 4-fluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzoic acid; 5-bromo-3,4-difluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzoic acid; 3,4-difluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzoic acid; 2-(4-methanesulfinyl-2-methyl-phenylamino)-4-nitro-benzoic acid; 3,4,5-trifluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzoic acid; 3,4-difluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzoic acid; 2-(2-methyl-4-methylsulfanyl-phenylamino)-4-nitro-benzoic acid;

3,4,5-trifluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzoic acid; 4-fluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzoic acid; 5-bromo-3,4-difluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzoic acid; 3,4,5-trifluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzoic acid; 4-fluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzoic acid; 5-bromo-3,4-difluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzoic acid; 3,4-difluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzoic acid; 2-(4-methanesulfonyl-2-methyl-phenylamino)-4-nitro-benzoic acid; N-cyclopropylmethoxy-4-fluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; 5-bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-4-nitro-benzamide; N-cyclopropylmethoxy-3,4,5-trifluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(2-methyl-4-methylsulfanyl-phenylamino)-4-nitro-benzamide; N-cyclopropylmethoxy-3,4,5-trifluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-4-fluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 5-bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4,5-trifluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; N-cyclopropylmethoxy-4-fluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 5-bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; and N-cyclopropylmethoxy-2-(4-methanesulfonyl-2-methyl-phenylamino)-4-nitro-benzamide.

90. A method of claim 59, wherein said MEK inhibitor has a structure selected from: 4-fluoro-N-hydroxy-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; 5-bromo-3,4-difluoro-N-hydroxy-2-(2-methyl-4-

methylsulfanyl-phenylamino)-benzamide; 3,4-difluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-4-nitro-benzamide; 3,4,5-trifluoro-N-hydroxy-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; 3,4-difluoro-N-hydroxy-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; N-hydroxy-2-(2-methyl-4-methylsulfanyl-phenylamino)-4-nitro-benzamide; 8: 3,4,5-trifluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 4-fluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 5-bromo-3,4-difluoro-N-hydroxy-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; 3,4,5-trifluoro-N-hydroxy-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; 4-fluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 5-bromo-3,4-difluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 3,4-difluoro-N-hydroxy-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; and N-hydroxy-2-(4-methanesulfonyl-2-methyl-phenylamino)-4-nitro-benzamide.

91. A method of claim 59, wherein said MEK inhibitor has a structure selected from: 3,4-difluoro-2-(4-imidazol-1-yl-2-methyl-phenylamino)-benzoic acid; N-cyclopropylmethoxy-3,4-difluoro-2-(4-imidazol-1-yl-2-methyl-phenylamino)-benzamide; 3,4-difluoro-N-hydroxy-2-(4-imidazol-1-yl-2-methyl-phenylamino)-benzamide; 3,4,5-trifluoro-2-(2-methyl-4-[1,2,5]thiadiazol-3-yl-phenylamino)-benzoic acid; N-cyclopropylmethoxy-3,4,5-trifluoro-2-(2-methyl-4-[1,2,5]thiadiazol-3-yl-phenylamino)-benzamide; 3,4,5-trifluoro-N-hydroxy-2-(2-methyl-4-[1,2,5]thiadiazol-3-yl-phenylamino)-benzamide; 2-[4-(4-chloro-[1,2,5]thiadiazol-3-yl)-2-methyl-phenylamino]-3,4,5-trifluoro-benzoic acid; 2-[4-(4-chloro-[1,2,5]thiadiazol-3-yl)-2-methyl-phenylamino]-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-[4-(4-chloro-[1,2,5]thiadiazol-3-yl)-2-methyl-phenylamino]-3,4,5-trifluoro-N-hydroxy-benzamide; 2-[4-[4-(2-dimethylamino-ethoxy)-[1,2,5]thiadiazol-3-yl]-2-methyl-phenylamino]-3,4,5-trifluoro-benzoic acid; N-cyclopropylmethoxy-3,4,5-trifluoro-2-[2-methyl-4-[4-(2-piperidin-1-yl-ethoxy)-[1,2,5]thiadiazol-3-yl]-

phenylamino}-benzamide; and 3,4,5-trifluoro-N-hydroxy-2-{2-methyl-4-[4-(2-morpholin-4-yl-ethoxy)-[1,2,5]thiadiazol-3-yl]-phenylamino}-benzamide.

92. The method of claim 59, wherein said MEK inhibitor has a
- 5 structure selected from: 5-bromo-2-(2-chloro-4-methylsulfanyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(2-chloro-4-methanesulfinyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(2-chloro-4-methanesulfonyl-phenylamino)-3,4,5-trifluoro-benzoic acid; 2-(2-chloro-methylsulfanyl-phenylamino)-3,4-difluoro-benzoic acid; 5-bromo-2-(2-chloro-4-methanesulfonyl-phenylamino)-3,4-
- 10 difluoro-benzoic acid; 2-(2-Chloro-4-methanesulfonyl-phenylamino)-3,4-difluoro-benzoic acid; 5-bromo-2-(2-chloro-4-methylsulfanyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-methanesulfinyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-methanesulfonyl-phenylamino)- N-cyclopropylmethoxy-3,4,5-trifluoro-
- 15 benzamide; 2-(2-chloro-4-methylsulfanyl-phenylamino)- N-cyclopropylmethoxy-3,4-difluoro-benzamide;
- 2-(2-chloro-4-methanesulfinyl-phenylamino)- N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 5-bromo-2-(2-chloro-4-methanesulfonyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-methylsulfanyl-
- 20 phenylamino)-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-(2-chloro-4-methanesulfonyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide;
- 2-[2-chloro 4-(3H-imidazol-1-yl)-phenylamino]-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-[1,2,5]thiadiazol-3-yl-phenylamino)-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-[4-(2-chloro-4-chloro-
- 25 [1,2,5]thiadiazol-3-yl)-phenylamino]-3,4,5-trifluoro-benzoic acid; 2-[2-chloro-4-(4-chloro-[1,2,5]thiadiazol-3-yl)-phenylamino]-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-{4-[4-(2-dimethylamino-ethoxy)-[1,2,5]thiadiazol-3-yl]-2-methyl-phenylamino}-3,4,5-trifluoro-benzoic acid; and 2-{2-chloro-4-[4-(2-piperidin-1-yl-ethoxy)-[1,2,5]thiadiazol-3-yl]-phenylamino}-N-
- 30 cyclopropylmethoxy-3,4,5-trifluoro-benzamide.

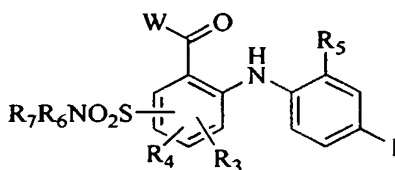
93. The method of claim 59, wherein said MEK inhibitor has a structure selected from: 2-(4-Ethynyl-2-methyl-phenylamino)-4-fluoro-benzoic acid; 5-Bromo-2-(4-ethynyl-2-methyl-phenylamino)-3,4-difluoro-benzoic acid; N-Cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-3,4-difluoro-benzamide; N-Cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-4-nitro-Benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-3,4,5-trifluoro-N-hydroxy-benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(4-Ethynyl-2-methyl-phenylamino)-4-nitro-benzoic acid; N-Cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-3,4,5-trifluoro-benzamide; 4-Fluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 5-Bromo-2-(4-ethynyl-2-methyl-phenylamino)-3,4-difluoro-N-hydroxy-benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-3,4,5-trifluoro-benzoic acid; N-Cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-4-fluoro-benzamide; 5-Bromo-N-cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-3,4-difluoro-benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-3,4-difluoro-N-hydroxy-benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-N-hydroxy-4-nitro-benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-4-fluoro-benzoic acid; N-Cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-4-fluoro-benzamide; and 4-Fluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide.

94. The method of claim 59, wherein said MEK inhibitor has a structure selected from: 2-(2-Chloro-4-ethynyl-phenylamino)-4-fluoro-benzoic acid; 5-Bromo-2-(2-chloro-4-ethynyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(2-Chloro-4-ethynyl-phenylamino)- N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-Chloro-4-ethynyl-phenylamino)- N-cyclopropylmethoxy-4-nitro-benzamide; 2-(2-Chloro-4-ethynyl-phenylamino)- N-hydroxy-3,4,5-trifluoro- benzamide; 2-(2-Chloro-4-ethynyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(4-Ethynyl-2-chloro-phenylamino)-4-nitro-benzoic acid; 2-(2-Chloro-4-ethynyl-phenylamino)- N-Cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-(2-chloro-4-methanesulfinyl-phenylamino)- 4-fluoro-N-hydroxy-benzamide; 5-Bromo-2-(4-ethynyl-2-chloro-phenylamino)-3,4-difluoro-N-hydroxy-benzamide; 2-(2-Chloro-4-ethynyl-phenylamino)-3,4,5-trifluoro-benzoic acid; 2-(2-Chloro-

4-ethynyl-phenylamino)- N-cyclopropylmethoxy-4-fluoro-benzamide; 5-Bromo-
 2-(2-chloro-4-ethynyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-
 benzamide; 2-(4-Ethynyl-2-chloro-phenylamino)-3,4-difluoro-N-hydroxy-
 benzamide; 2-(4-Ethynyl-2-chloro-phenylamino)-N-hydroxy-4-nitro-
 5 benzamide; 2-(2-Chloro-4-ethynyl-phenylamino)-4-fluoro-benzoic acid; 2-(2-
 Chloro-4-ethynyl-phenylamino)- N-cyclopropylmethoxy-4-fluoro-benzamide; 2-
 (2-Chloro-4-methanesulfinyl-phenylamino)- 4-fluoro-N-hydroxy-benzamide;
 and 2-(2-chloro-4-imidazol-1-yl-phenylamino)- 3,4-Difluoro-benzoic acid.

10 95. A method for treating chronic pain, said method comprising
 administering to a subject in need of such treatment a composition comprising
 a MEK inhibitor selected from a compound of formula (I)C:

15



(I)C

20

25 wherein

W is OR₁, NR₂OR₁, NR_AR_B, NR₂NR_AR_B, or NR₂(CH₂)₂₋₄ NR_AR_B;

R₁ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl,
 30 (phenyl)C₁₋₄ alkyl, (phenyl)C₃₋₄ alkenyl, (phenyl)C₃₋₄ alkynyl, (C₃₋₈
 cycloalkyl)-

C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkenyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkynyl or (CH₂)₂₋₄NR_AR_B;

- 5 R₂ is H, phenyl, C₁₋₄ alkyl, C₃₋₄ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, or (C₃₋₈ cycloalkyl)-C₁₋₄ alkyl;

- R_A is H, C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C₁₋₄ alkyl, (aminosulfonyl)C₁₋₆ alkyl, (aminosulfonyl)C₃₋₆ cycloalkyl, or [(aminosulfonyl)C₃₋₆ cycloalkyl]C₁₋₄ alkyl;
- 10

- 15 R_B is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, or C₆₋₈ aryl;

R₃ is H, F, Cl, Br, or NO₂;

R₄ is H or F;

20

R₅ is H, methyl or Cl;

- R₆ is H, C₁₋₄ alkyl, hydroxyethyl, hydroxypropyl, (CH₂)₂₋₄(NR_CR_D), phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl or CH₂Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;
- 25

- R₇ is H, C₁₋₄ alkyl, hydroxyethyl, hydroxypropyl, (CH₂)₂₋₄(NR_CR_D), phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or CH₂Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;
- 30

each of R_C and R_D is independently selected from H, C₁₋₆ alkyl, C₃₋₄ alkenyl,

C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, C₃₋₆ heterocyclic radical, and phenyl; NR_CR_D can also be selected from morpholinyl, piperazinyl, pyrrolidinyl, or piperadinyl;

wherein each hydrocarbon radical or heterocyclic radical above is
5 optionally substituted with between 1 and 3 substituents independently
selected from halo, C₁₋₄ alkyl, C₃₋₆ cycloalkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl,
phenyl, hydroxy, amino, (amino)sulfonyl, and NO₂, wherein each substituent
alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with
10 between 1 and 3 substituents independently selected from halo, C₁₋₂ alkyl,
hydroxy, amino, and NO₂;

or a pharmaceutically-acceptable salt or C₁₋₆ ester thereof.

96. The method of claim 95, wherein said chronic pain is selected
15 from neuropathic pain, idiopathic pain, and pain associated with chronic
alcoholism, vitamin deficiency, uremia, or hypothyroidism.

97. The method of claim 96, wherein said chronic pain is a type of
neuropathic pain.

98. The method of claim 97, wherein said neuropathic pain is
20 associated with one of the following: inflammation, postoperative pain,
phantom limb pain, burn pain, gout, trigeminal neuralgia, acute herpetic and
postherpetic pain, causalgia, diabetic neuropathy, plexus avulsion, neuroma,
vasculitis, viral infection, crush injury, constriction injury, tissue injury, limb
amputation, post-operative pain, arthritis pain, and any other nerve injury
25 between the peripheral nervous system and the central nervous system,
inclusively.

99. The method of claim 96, wherein said chronic pain is associated
with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

30

100. The method of claim 96, wherein said chronic pain is associated with idiopathic pain.

5 101. The method of claim 95, wherein said chronic pain is associated with inflammation.

102. The method of claim 95, wherein said chronic pain is associated with arthritis.

10 103. The method of claim 95, wherein said chronic pain is associated with post-operative pain.

15 104. A method of claim 95, wherein the sulfamoyl group is *meta* to W(CO)- and *para* to the bridging NH.

105. A method of claim 95, wherein the sulfamoyl group is *para* to W (CO)- and *meta* to the bridging NH.

20 106. A method of claim 95, wherein R₄ is fluoro.

107. A method of claim 95, where R₃ is fluoro.

108. A method of claim 95, where R₃ is H.

25 109. A method of claim 95, wherein W is OH.

110. A method of claim 95, wherein W is NR₂OR₁.

30 111. A method of claim 109, wherein each of R₃ and R₄ is fluoro.

112. A method of claim 95, wherein R₁ has at least one hydroxy substituent.

113. A method of claim 95, wherein R_1 is H, methyl, ethyl, propyl, isopropyl, isobutyl, benzyl, phenethyl, allyl, C_{3-5} alkenyl, C_{3-5} alkynyl, C_{3-6} cycloalkyl, $(C_{3-5}$ cycloalkyl) C_{1-2} alkyl, or $(C_{3-5}$ heterocyclic radical)-
5 C_{1-2} alkyl.
114. A method of claim 113, wherein R_1 is H or $(C_{3-4}$ cycloalkyl)-
 C_{1-2} alkyl.
- 10 115. A method of claim 95, wherein R_2 is H, methyl, C_{3-4} alkynyl, C_{3-5} cycloalkyl, or $(C_{3-5}$ cycloalkyl)methyl.
116. A method of claim 95, wherein R_A is H, methyl, ethyl, isobutyl, hydroxyethyl, hydroxypropyl, cyclopropylmethyl, cyclobutylmethyl, C_{3-4}
15 alkynyl, phenyl, 2-piperidin-1-yl-ethyl, 2,3-dihydroxy-propyl, 3-[4-(2-hydroxyethyl)-piperazin-1-yl]-propyl, 2-pyrrolidin-1-yl-ethyl, or 2-diethylamino-ethyl; and R_B is H; or where R_B is methyl and R_A is phenyl.
117. A method of claim 95, wherein R_7 is $(CH_2)_{2-4}(NR_C R_D)$.
20
118. A method of claim 95, wherein $NR_C R_D$ is selected from morpholinyl, piperazinyl, pyrrolidinyl, or piperadinyl.
119. A method of claim 95, wherein R_5 is methyl or chloro.
25
120. A method of claim 95, wherein said MEK inhibitor has a structure selected from: 2-(2-chloro-4-iodo-phenylamino)-4-sulfamoyl-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-N-hydroxy-4-sulfamoyl-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-sulfamoyl-benzamide;
30 2-(2-chloro-4-iodo-phenylamino)-4-(2-morpholin-4-yl-ethylsulfamoyl)-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-N-hydroxy-4-(2-morpholin-4-yl-ethylsulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-

- cyclopropylmethoxy-4-(2-morpholin-4-yl-ethylsulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-5-sulfamoyl-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-5-sulfamoyl-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-sulfamoyl-
- 5 benzamide; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-5-(2-morpholin-4-yl-ethylsulfamoyl)-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-5-(2-morpholin-4-yl-ethylsulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(2-morpholin-4-yl-ethylsulfamoyl)-benzamide; 5-(bis-pyridin-3-ylmethyl-sulfamoyl)-3,4-difluoro-2-
- 10 (4-iodo-phenylamino)-benzoic acid; 5-(bis-pyridin-3-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-(methyl-pyridin-3-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-[(pyridin-3-ylmethyl)-sulfamoyl]-benzamide; N-
- 15 cyclopropylmethoxy-5-[(3-diethylamino-propyl)-pyridin-3-ylmethyl-sulfamoyl]-3,4-difluoro-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-3-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-5-(ethyl-pyridin-3-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-iodo-phenylamino)-benzamide; N-
- 20 cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-3-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; 5-(bis-pyridin-2-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-iodo-phenylamino)-benzoic acid; 5-(bis-pyridin-2-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-
- 25 phenylamino)-5-(methyl-pyridin-2-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-[(pyridin-2-ylmethyl)-sulfamoyl]-benzamide; 5-(bis-pyridin-3-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid; 5-(bis-pyridin-3-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-
- 30 phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-(methyl-pyridin-3-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-[(pyridin-

- 3-ylmethyl)-sulfamoyl]-benzamide; N-cyclopropylmethoxy-5-[(3-diethylamino-propyl)-pyridin-3-ylmethyl-sulfamoyl]-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-3-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-5-(ethyl-pyridin-3-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-3-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; 5-(bis-pyridin-2-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid; 5-(bis-pyridin-2-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-(methyl-pyridin-2-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-[(pyridin-2-ylmethyl)-sulfamoyl]-benzamide; 5-(bis-pyridin-3-ylmethyl-sulfamoyl)-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-benzoic acid; 5-(bis-pyridin-3-ylmethyl-sulfamoyl)-2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(methyl-pyridin-3-ylmethyl-sulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(pyridin-3-ylmethyl)-sulfamoyl]-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-5-[(3-diethylamino-propyl)-pyridin-3-ylmethyl-sulfamoyl]-3,4-difluoro-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-3-ylmethyl-sulfamoyl]-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-5-(ethyl-pyridin-3-ylmethyl-sulfamoyl)-3,4-difluoro-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-3-ylmethyl-sulfamoyl]-benzamide; 5-(bis-pyridin-2-ylmethyl-sulfamoyl)-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-benzoic acid; 5-(bis-pyridin-2-ylmethyl-sulfamoyl)-2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(methyl-pyridin-2-ylmethyl-sulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-

cyclopropylmethoxy-3,4-difluoro-5-[(pyridin-2-ylmethyl)-sulfamoyl]-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-2-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-2-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; 5-(benzyl-pyridin-2-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-[(pyridin-4-ylmethyl)-sulfamoyl]-benzamide; N-cyclopropylmethoxy-5-(ethyl-pyridin-4-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-(methyl-pyridin-4-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-(methyl-phenyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-phenylsulfamoyl-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-(pyridin-3-ylsulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-2-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-2-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; 5-(benzyl-pyridin-2-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-[(pyridin-4-ylmethyl)-sulfamoyl]-benzamide; N-cyclopropylmethoxy-5-(ethyl-pyridin-4-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-(methyl-pyridin-4-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-

cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-(methyl-phenyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-phenylsulfamoyl-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-(pyridin-3-ylsulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-2-ylmethyl-sulfamoyl]-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-2-ylmethyl-sulfamoyl]-benzamide; 5-(benzyl-pyridin-2-ylmethyl-sulfamoyl)-2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(pyridin-4-ylmethyl)-sulfamoyl]-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-5-(ethyl-pyridin-4-ylmethyl-sulfamoyl)-3,4-difluoro-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(methyl-pyridin-4-ylmethyl-sulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-4-ylmethyl-sulfamoyl]-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(methyl-phenyl-sulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-phenylsulfamoyl-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(pyridin-3-ylsulfamoyl)-benzamide; N-cyclopropylmethoxy-2-(4-iodo-phenylamino)-4-phenylsulfamoyl-benzamide; N-cyclopropylmethoxy-2-(4-iodo-phenylamino)-4-(pyridin-3-ylsulfamoyl)-benzamide; N-cyclopropylmethoxy-2-(4-iodo-phenylamino)-4-[(pyridin-3-ylmethyl)-sulfamoyl]-benzamide; 4-(bis-pyridin-3-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-4-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(4-iodo-phenylamino)-4-(methyl-pyridin-3-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-4-[(3-diethylamino-propyl)-pyridin-3-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(4-iodo-2-

methyl-phenylamino)-4-phenylsulfamoyl-benzamide; N-cyclopropylmethoxy-2-
 (4-iodo-2-methyl-phenylamino)-4-(pyridin-3-ylsulfamoyl)-benzamide; N-
 cyclopropylmethoxy-2-(4-iodo-2-methyl-phenylamino)-4-[(pyridin-3-ylmethyl)-
 sulfamoyl]-benzamide; 4-(bis-pyridin-3-ylmethyl-sulfamoyl)-N-
 5 cyclopropylmethoxy-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-
 cyclopropylmethoxy-4-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-
 iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(4-iodo-2-
 methyl-phenylamino)-4-(methyl-pyridin-3-ylmethyl-sulfamoyl)-benzamide; N-
 cyclopropylmethoxy-4-[(3-diethylamino-propyl)-pyridin-3-ylmethyl-sulfamoyl]-
 10 2-(4-iodo-2-methyl-phenylamino)-benzamide; 2-(2-chloro-4-iodo-
 phenylamino)-N-cyclopropylmethoxy-4-phenylsulfamoyl-benzamide; 2-(2-
 chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-(pyridin-3-ylsulfamoyl)-
 benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-
 [(pyridin-3-ylmethyl)-sulfamoyl]-benzamide; 4-(bis-pyridin-3-ylmethyl-
 15 sulfamoyl)-2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-
 benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-[(2-
 hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-benzamide; 2-(2-chloro-4-iodo-
 phenylamino)-N-cyclopropylmethoxy-4-(methyl-pyridin-3-ylmethyl-sulfamoyl)-
 benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-[(3-
 20 diethylamino-propyl)-pyridin-3-ylmethyl-sulfamoyl]-benzamide; and 5-[bis-(4-
 methoxy-benzyl)-sulfamoyl]-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-
 benzoic acid; and 2-(2-chloro-4-iodo-phenylamino)-5-dimethylsulfamoyl-3,4-
 difluoro-benzoic acid methyl ester.

25 121. The method of claim 95, wherein said MEK inhibitor has a
 structure selected from: PD 298458, N-Allyloxy-2-(2-chloro-4-iodo-
 phenylamino)-3,4-difluoro-5-(4-methyl-piperazine-1-sulfonyl)-benzamide; PD
 298459, N-Allyloxy-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-5-(methyl-
 phenyl-sulfamoyl)-benzamide; PD 298460, 5-(Allyl-methyl-sulfamoyl)-N-
 30 allyloxy-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-benzamide; PD 298463,
 1-[5-Allyloxycarbamoyl-4-(2-chloro-4-iodo-phenylamino)-2,3-difluoro-
 benzenesulfonyl]-piperidine-3-carboxylic acid amide; PD 298464, N-Allyloxy-

2-(2-chloro-4-iodo-phenylamino)-5-[(3-dimethylamino-propyl)-methyl-sulfamoyl]-3,4-difluoro-benzamide; PD 298465, N-Allyloxy-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-5-(4-pyridin-2-yl-piperazine-1-sulfonyl)-benzamide; and PD 298467, N-Allyloxy-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-5-(methoxy-methyl-sulfamoyl)-benzamide.

122. The method of claim 1, wherein said MEK inhibitor has a structure selected from: 2-(2-chloro-4-iodo-phenylamino)-*N*-cyclopropylmethoxy-3,4-difluoro-benzenesulfonamide; and 2-(2-chloro-4-iodo-phenylamino)-cyclopropylmethoxy-3,4-difluoro-benzenesulfonamide.

123. The method of claim 27, wherein said MEK inhibitor has a structure selected from: 2,4-bis-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-benzoic acid.

124. The method of claim 59, wherein said MEK inhibitor has a structure selected from: 2-(4-ethynyl-2-methyl-phenylamino)-4-fluoro-benzoic acid; and 2-(3',5'-dichloro-biphenyl-4-ylamino)-benzoic acid.

125. The method of claim 95, wherein said MEK inhibitor has a structure selected from: 2-(2-chloro-4-iodo-phenylamino)-*N*-cyclopropylmethoxy-3,4-difluoro-5-sulfamoyl-benzamide; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-*N*-hydroxy-5-sulfamoyl-benzamide; *C*-(2-chloro-4-iodo-phenylamino)-*N*-cyclopropylmethoxy-dimethylsulfamoyl-difluoro-benzamide; *N*-cyclopropylmethoxy-dimethylsulfamoyl-difluoro-*C*-(4-iodo-2-methyl-phenylamino)-benzamide; and *C*-(2-chloro-4-iodo-phenylamino)-difluoro-(methoxy-methyl-sulfamoyl)-*N*-(2-morpholin-4-yl-ethoxy)benzamide.